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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,097	04/13/2004	Cynthia C. Bamdad	M1015.70013US01	3158

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EXAMINER	
DO, PENSEE T	
ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
07/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Office Action Summary	Application No.	Applicant(s)	
	10/823,097	BAMDAD ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *485-502 and 504* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *485-502, 504* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 13, 2007 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 485-504 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 485 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the signaling entity bound to one of the beads. The specification of the present invention requires a signaling entity bound to either beads (see pg. 27, lines 15-20).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 485 is rejected under 35 U.S.C. 103(a) as being unpatentable over by Liberti et al. (US 5,108,933) in view of Sigal (US 6,319,670).

Liberti teaches manipulating colloids via magnetic separation. The method is using a first colloidal protein magnetite (first colloidal particle coated with first protein) and a second colloidal protein magnetite having a binding affinity for a determinant on the first colloidal protein magnetite. (see col. 18, line 66-col. 19, line 2). Separation takes place before determining the immobilization of the first colloid particle with respect to the second colloidal particle. (see col. 18, lines 44-46). Liberti also teaches the use of gold colloidal (col. 11, line 35).

However, Liberti fails to teach a self-assembled monolayer.

Sigal et al. teaches on col. 7, lines 62-68 that assay ligands can be adsorbed onto surfaces by modification of the ligands with moieties that are known to strongly adsorb on the surface, for example thiols will facilitate adsorption of gold. Alternatively, the assay-ligand may be immobilized by adsorption and/or covalent attachment to a "binding layer" coated on the surface of the particle. For example, an assay-ligand may be covalently attached to an oxide surface (e.g., silica or tin oxide) by attachment to

functional groups introduced on the surface of the particle (these functional groups may be introduced by methods well-known in the art, e.g., by coating the particle with a self-assembled layer of a functionalized monomer such as a silane. Similarly, an assay-ligand may be covalently attached to the gold surface of a gold particle by coating the particle by reaction with a functionalized thiol (e.g., to form a self-assembled monolayer). (see col. 8, lines 8-20).

Since it is well known in the art, as taught by Sigal, that a self-assembled monolayer such as thiols layer on gold particles is a layer of moieties that are known to strongly adsorb ligands to the surface of the gold particles, it would have been obvious to one of ordinary skills in the art to coat the gold particles of Liberti with a SAM as taught by Sigal. Self- assembled monolayer is also known as an orderly layer which, when bound with ligands, provides discrete binding sites on the particles for the target analytes.

Claim 485 is rejected under 35 U.S.C. 103(a) as being unpatentable over Masson et al. (US 4,279,617) in view of Sigal (US 6,319,670).

Masson teaches a particle agglutination assay for antigens, antibodies and other binding proteins using two different, microscopic or submicroscopic particulate reagents. The first particulate reagent binds with the antigen or antibody under assay, and then the second particulate reagent which has a specific binding member attached thereto is added which binds only to those first reagent particles which have bound to the antigen or antibody under assay, so causing agglutination. The free unbound first and second

particles are assayed to indicate the presence and/or amount of the antigen/antibody under assay. (see abstract, col. 1, line 64-col. 2, line 67; col. 4, lines 59-63). Determining the immobilization of the first and second particles is equivalent to the counting of the non-bound particles. The specification of the present invention describes that colloidal particles are nanoparticles including inorganic, organic, polymeric, ceramic, semiconductor, metallic (gold), non-metallic, etc. (see page 22, lines 4-11). The particles of Masson are latex which are less than 15 microns. (col. 2, lines 31-35).

However, Masson fails to teach a self-assembled monolayer.

Sigal et al. teaches on col. 7, lines 62-68 that assay ligands can be adsorbed onto surfaces by modification of the ligands with moieties that are known to strongly adsorb on the surface, for example thiols will facilitate adsorption of gold. Alternatively, the assay-ligand may be immobilized by adsorption and/or covalent attachment to a "binding layer" coated on the surface of the particle. For example, an assay-ligand may be covalently attached to an oxide surface (e.g., silica or tin oxide) by attachment to functional groups introduced on the surface of the particle (these functional groups may be introduced by methods well-known in the art, e.g., by coating the particle with a self-assembled layer of a functionalized monomer such as a silane. Similarly, an assay-ligand may be covalently attached to the gold surface of a gold particle by coating the particle by reaction with a functionalized thiol (e.g., to form a self-assembled monolayer). (see col. 8, lines 8-20).

Since it is well known in the art, as taught by Sigal, that a self-assembled monolayer such as thiols layer on gold particles is a layer of moieties that are known to

strongly adsorb ligands to the surface of the gold particles, it would have been obvious to one of ordinary skills in the art to coat the gold particles of Masson with a SAM as taught by Sigal. Self- assembled monolayer is also known as an orderly layer which, when bound with ligands, provides discrete binding sites on the particles for the target analytes.

Claims 485-487, 489-502 and 504 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US 6,984,491) in view of Sigal (US 6,319,670).

Mirkin teaches a method of immobilizing colloid particles comprising allowing a first nanoparticle (colloid) conjugated to first oligonucleotides and a second nanoparticle (colloid) conjugated to second oligonucleotides to bind to each other via the binding of first and second oligonucleotides (see col. 4, line 65-col. 5, line 18). With respect to claims 486 and 487, Mirkin teaches that gold particles may be attached to oligonucleotides using biotin-labeled oligonucleotides and streptavidin-gold conjugate (affinity tag interaction) (see col. 130, lines 9-55). Mirkin also teaches that the gold particles can be functionalized with carboxylic acids (carboxylate group) (see col. 38 line 64). With respect to claim 489, the oligonucleotides interaction is a biological interaction. With respect to claim 492, oligonucleotides are synthetic molecules. (example 17). With respect to claim 493, the nanoparticles are gold colloid particles. (see col. 71, line 34). With respect to claims 494 and 495, Mirkin teaches that the oligonucleotides on either nanoparticles are labeled with an energy acceptor or donor which are fluorescent molecules (equivalent to emissive or absorptive species of the claimed invention). (see

col. 7, line 30). With respect to claims 496, 498, 500, and 504, Mirkin teaches that the first oligonucleotides have a sequence complement to a first portion of the sequence of a target nucleic acid, and the second oligonucleotides have a sequence complement to a second portion of the sequence of the target nucleic acid. The nucleic acid is contacted with the two types of nanoparticles having first and second oligonucleotides under conditions for hybridization of the oligonucleotides with the nucleic acid. (common entity-biological material) (see col. 4, line 65-col. 5, line 18). The nucleic acid forms a aggregate of the two nanoparticles. Thus, it is an aggregate forming species. With respect to claim 497, Mirkin teaches the two binding species bind to a common entity which is a colloid particle in figure 13B, the aggregate of nanoparticles. With respect to claims 499 and 501, Mirkin teaches the analyte is a drug (see col. 27, lines 10-12). With respect to claim 502, Mirkin teaches that the analyte can be an enzyme. (see col. 27, lines 40-42).

However, Mirkin fails to teach a self-assembled monolayer and that the first and second species are protein and that the binding interaction is between a protein and a nucleic acid.

Sigal et al. teaches on col. 7, lines 62-68 that assay ligands can be adsorbed onto surfaces by modification of the ligands with moieties that are known to strongly adsorb on the surface, for example thiols will facilitate adsorption of gold. Alternatively, the assay-ligand may be immobilized by adsorption and/or covalent attachment to a "binding layer" coated on the surface of the particle. For example, an assay-ligand may be covalently attached to an oxide surface (e.g., silica or tin oxide) by attachment to

functional groups introduced on the surface of the particle (these functional groups may be introduced by methods well-known in the art, e.g., by coating the particle with a self-assembled layer of a functionalized monomer such as a silane. Similarly, an assay-ligand may be covalently attached to the gold surface of a gold particle by coating the particle by reaction with a functionalized thiol (e.g., to form a self-assembled monolayer). (see col. 8, lines 8-20).

Since it is well known in the art, as taught by Sigal, that a self-assembled monolayer such as thiols layer on gold particles is a layer of moieties that are known to strongly adsorb ligands to the surface of the gold particles, it would have been obvious to one of ordinary skills in the art to coat the gold particles of Mirkin with a SAM as taught by Sigal. Self- assembled monolayer is also known as an orderly layer which, when bound with ligands, provides discrete binding sites on the particles for the target analytes.

Regarding claims 490 and 491, Mirkin has been discussed above for teaching the present invention except that Mirkin discusses on col. 1, lines 55-60, that methods have been reported for making nanoparticles (Quantum dots) water soluble, allowing the immobilization of protein structure on the quantum dot surface. One involves encapsulation of the core-shell structures with a silica layer.

Thus, it would have been obvious to one of ordinary skills in the art to immobilize protein on the nanoparticles and allow the proteins to bind to each other to form aggregate or to bind to a common entity such as a nucleic acid to study protein-protein interaction of a sample in order to diagnose a disease or condition.

Claim 488 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin in view of Sigal as applied to claim 485 , and further in view of Went (US 6,150,179).

Mirkin and Sigal have been discussed above.

However, Mirkin and Sigal fail to teach that the species fastened to the colloid particle via a metal binding tag.

Went teaches incorporate metal affinity binding tag such as His-tag into proteins so that the proteins can bind to solid phase. (see col. 20, lines 39-40; col. 58, line 49).

It would have been obvious to one of ordinary skills in the art to use the metal binding tag taught by Went as an affinity binding tag to bind the oligonucleotides or proteins to the nanoparticles because the nanoparticles are metals and thus such tag would bind with high affinity to the nanoparticles since it is a metal binding tag.

Response to Arguments

Applicant's arguments filed December 13, 2007 have been fully considered but they are not persuasive.

With respect to the 112, 2nd paragraph rejection, Applicants argue that one of ordinary skills in the art would be able to detect the immobilization using whichever technique may be available.

This is not found persuasive because there is no label attached to the complex and detection technique depends on the label. Thus, without any label, one of ordinary skill in the art would not be able to detect anything.

With respect to the ODP rejection over US application 10/763,810, since the application is abandoned. The ODP rejection is withdrawn herein.

With respect to the 102 and 103 rejections by Liberti, Masson and Mirkin, Applicants arguments are moot in view of the new grounds of rejection because the references fail to teach a self-assembled monolayer.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Pensee T. Do/
Examiner, Art Unit 1641
March 27, 2008

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641